## REMARKS

In view of the foregoing amendments and the following representations, reconsideration and allowance of the above-identified application is respectfully requested.

**Status of the Claims:**

Claims 1-37 have been cancelled without prejudice.

Claims 38-55 are currently pending in the application. Claim 38 has been amended to employ the same description of the first pellet and second pellet employed in independent claims 51 and 52.[1]

**35 U.S.C. § 103(a):**

On page 2 of the Office Action, the Examiner rejected claims 38-55 under 35 U.S.C. §103(a) as being unpatentable over the teachings of Midha et al., WO 00/59479 (hereinafter "Midha") in view of Percel et al., United States Published Patent Application No. 2001/0046964 (hereinafter "Percel").

Reconsideration and withdrawal of this rejection is respectfully requested.

The pending claims recite a bupropion tablet or capsule that is administered to a patient once a day to produce a specific *in vivo* plasma profile. The claimed tablet or capsule comprises three separate and distinct bupropion components:

1) an immediate release component that releases the bupropion upon administration of the composition to a patient;

2) a first pellet comprising a first core containing a pharmaceutically acceptable salt of bupropion and an enteric coating applied to the first core so the first pellet releases the bupropion in the upper gastrointestinal tract of a human patient (at a pH of about 4.8 [claims 53-55]); and

[1] Claims 40 and 41 were also amended to correct typographical errors.

3) a second pellet comprising a second core containing a pharmaceutically acceptable salt of bupropion and a sustained release coating applied to the second core wherein the sustained release coating comprises a water insoluble polymer so the second pellet releases the bupropion in the lower gastrointestinal tract of a human patient (at a pH of about 7 [claims 53-55]).

It is respectfully submitted that the pending claims are patentable over the combination of Midha and Percel because a skilled artisan, reviewing the references, would not be led to the claimed three-component bupropion dosage form that exhibits the recited *in vivo* plasma profile with an expectation of success.

Midha teaches pulsatile delivery systems and states "a precise and effective pulsatile drug delivery system is difficult to formulate and manufacture". *See* Midha at p. 2, lines 3-4. Midha further provides a list of membrane forming materials that may be used to provide the pulsatile drug release on pages 8-9 and describes the various types of dosage forms such as coated tablets, coated beads or matrix forms on page 9. With respect to the coated tablets and coated beads, Midha teaches that pulsatile delivery is obtained by varying the coating thickness and not the coating material as recited in the pending claims. Specifically Midha teaches:

> To bring about the desired pulsatile release profile for a dosage form comprised of encapsulated tablets, the first tablet is provided with little or no coating material, the second tablet is provided with some degree of coating material, the coating weight of a third tablet is still higher, and so on. Analogously, for encapsulated dosage forms in which the drug-containing dosage units are beads or particles, a first fraction of beads or particles is provided with little or no coating material, a second fraction is provided with some degree of coating material, the coating weight of a third fraction is still higher, etc. For example, when the dosage form contains three tablets (or, analogously, three groups of drug-containing particles or beads), the first tablet, which releases drug substantially immediately, may have a total coating weight of less than about 10%, preferably less than about 8%, the second tablet may have a total coating weight in the range of approximately 10% to 30%, preferably 15% to 25%, and the third tablet, if present, may have a total coating weight in the range of approximately 15% to 65%, preferably 20% to 65%.

*See* Midha at p. 9, lines 5-17. Examples 1 and 2 of Midha further confirm the above teaching by exemplifying a three-tablet dosage form and a pellet dosage form comprising three types of pellets.

The release of the drug from the dosage forms described in Example 1 and 2 of Midha is controlled by varying the coating weight applied to the tablets or pellets and not the coating material. *See* Midha at pp. 16-18. Although Midha does mention bupropion as a potential drug, Midha fails to provide the skilled artisan with any guidance for selecting the amount of bupropion to be employed and the ratio of modified release pellets to be employed in a dosage form to obtain an *in vivo* plasma profile suitable for once-a-day administration.

Percel teaches a pulsatile dosage form similar to Midha that employs two or more coated particles with different release rates. The different release rates are obtained by varying the coating weight and not the coating composition on the particles. *See* Percel at ¶ 19 and Examples 1, 2 and 4 which report different release profiles based upon coating weight. Applicants do not dispute that Percel teaches enteric coatings and sustained release coatings, however, both the enteric coating and the sustained release coating taught by Percel are applied to the same particle, not separate particles. Percel, like Midha, mentions bupropion as a potential drug, but fails to provide the skilled artisan with any guidance for selecting the amount of bupropion to be employed and the ratio of modified release pellets to be employed in a dosage form to obtain an *in vivo* plasma profile suitable for once-a-day administration.

Applicants respectfully submit that the combination of Midha and Percel would not lead a skilled artisan to the presently claimed invention. The combination of Midha and Percel would motivate a skilled artisan to prepare a multi-pellet dosage form wherein the same coating was applied to pellet cores but at varying coating weights to modify the release rate. The combined teachings of Midha and Percel would not suggest or motivate a skilled artisan to prepare a three-component system as recited in the pending claims wherein the drug release is controlled by separate and distinct pellets with separate and distinct coatings, i.e., an enteric coated pellet and a

sustained release coated pellet. Moreover, the combined teachings of Midha and Percel fail to provide the skilled artisan with any guidance for selecting the amount of bupropion and ratio of coated bupropion pellets to obtain a once-a-day bupropion tablet or capsule that exhibits the *in vivo* plasma profile recited in the pending claims.

Because the combination of Midha and Percel fail to suggest a once-a-day bupropion tablet or capsule with an enteric coated pellet and a separate and distinct sustained release coated pellet, as required by the pending claims, Applicants submit that the pending claims are patentable over the combination of Midha and Percel.

In light of the foregoing amendments and remarks, Applicants respectfully submit that the claims of the present application are in proper form for allowance. Early and favorable consideration is therefore earnestly solicited and respectfully requested. If the Examiner does not believe the pending claims are in proper form for allowance, Applicants invite the Examiner to call the undersigned to discuss ways to further expedite prosecution of this application.

Respectfully submitted,

/martin p. endres/

Martin P. Endres
Reg. No. 35,498

**MAILING ADDRESS**
FLOREK & ENDRES, PLLC.
1156 Avenue of the Americas
New York, NY 10036
(212) 997-1000